NORTH DAKOTA
DEPARTMENT *of* HEALTH

Health Alert Network

Feb. 14, 2014 **Health Advisory**

Guidance for Providers on Syphilis Diagnosis and Treatment

Syphilis remains an important public health problem in the United States and in North Dakota. This infection can be difficult to diagnose and manage from both a clinical and a public health perspective. Clinical management depends on the stage of syphilis diagnosed. Syphilis may present as primary, secondary, tertiary (gummatous) or cardiac and/or neurologic disease. Syphilis also has periods of latency characterized by the absence of any signs or symptoms.

Epidemiology

The number of cases of syphilis being reported in North Dakota has increased since 2011. In 2011, two cases of primary or secondary syphilis were reported to the North Dakota Department of Health. In 2012 the number of cases of primary or secondary cases increased to four. Preliminary numbers for 2013 for primary, secondary or early latent syphilis cases is 13. An additional 13 cases of latent syphilis were reported in 2013.

In 2013, 38 percent of early syphilis cases were located in Sioux County. Of all the cases reported in 2013, 42 percent were American Indian, 35 percent were white and 19 percent were black. Eighteen (69 percent) of the cases were male. Four individuals had been co-infected with syphilis and HIV. In the United States, 75 percent of all primary and secondary cases occur in men who have sex with men. In North Dakota, the majority of cases were reported in heterosexual individuals. Seven (27 percent) of the cases were reported to be men who have sex with men.

Staging of Syphilis

Based on clinical findings, syphilis has been divided into a series of stages that are used to guide treatment and follow-up. Primary syphilis usually presents itself as an ano-genital sore (primary chancre) with a raised border that is often reported as painless. This chancre is contagious, as it will have *treponema pallidum* on its surface. Secondary syphilis usually presents as a rash that may take on several different appearances. The rash may appear as rough, red or reddish brown spots that may be found on the palms of the hand or the soles of the feet and usually do not cause

itching. However, rashes with different appearances may occur on other parts of the body and may resemble rashes caused by other diseases. Secondary syphilis may also present as large, raised, gray or white lesions in moist areas; these lesions are contagious.

In addition to rashes and lesions, symptoms presented might also include fever, swollen lymph glands, sore throat, patchy hair loss, headaches, weight loss, muscle aches and fatigue. The symptoms of primary and secondary syphilis will go away with or without treatment, but without treatment, the infection will progress to the late stages of disease. Latent infections are defined by the lack of clinical manifestations. Early latent syphilis is defined as having acquired syphilis within the past year but there are no symptoms of the disease. Tertiary syphilis can either present as gummatous lesions or as cardiovascular infections. Neurosyphilis can occur at any time during a syphilis infection.

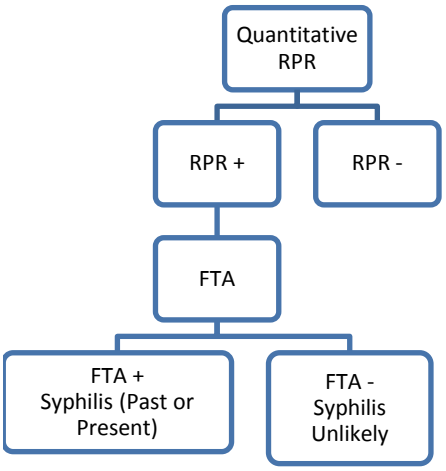
The period of latency between primary and secondary may not exist or may be measured in weeks. The latency period after secondary syphilis may be long, often measured in years.

Testing

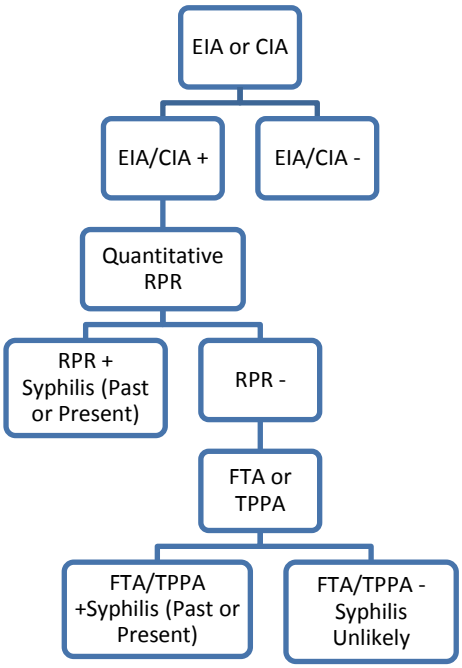
Today's syphilis diagnostics largely depend on serum tests to detect nontreponemal and treponemal antibodies. Historically, the syphilis diagnostic algorithm started with a nontreponemal test such as the RPR or the VDRL. If reactive, the results would be quantified through dilutions and reported out as a titer. The reactive nontreponemal test would then be followed by a treponemal test such as the FTA-ABS or the TP-PA. If the treponemal test is reactive, a syphilis diagnosis is confirmed.

EIAs and CIA that detect treponemal antibodies have become popular because they are sensitive, specific and can be done on an automated platform. However, a single EIA or CIA result is not adequate for the diagnosis of syphilis. Because of the low prevalence of syphilis in North Dakota, the positive predictive value of EIAs and CIAs is low. Persons who have a reactive or positive EIA or CIA test should be tested with a nontreponemal test and if reactive, should be considered to have a syphilis infection. If the nontreponemal test is non-reactive, a second treponemal test such as the FTA-ABS or TP-PA should be performed. If the second treponemal test is positive, untreated persons should be offered treatment. Please see the diagrams below for traditional and reverse sequence (EIA/CIA) testing algorithms.

Traditional Screening



Reverse Sequence



The value of quantified nontreponemal tests is often associated with disease activity. Titers generally increase through primary and early latent syphilis and often peak in secondary syphilis. Titers may decrease during periods of latency, even when cases have not been treated. Treatment early in the incubation period or in early primary syphilis may prevent a non-treponemal test from becoming reactive. Treatment late in infection often results in a serofast condition with low level titers such as 1:1 or 1:2 remaining throughout life. Treatment can be monitored using non-treponemal titers. Successful treatment should result in a four-fold (two dilution) decrease in titer (ie: 1:8 to 1:2 or 1:256 to 1:64). Ideally, nontreponemal tests should be performed by the same laboratory using the same methods to provide the most consistent and comparable results. If your laboratory does not routinely quantify reactive nontreponemal tests, you may have to specify you want such tests quantified and the titer reported.

Treatment

Benzathine penicillin G (ie. Bicillin, LA™) remains the preferred treatment for syphilis. Early syphilis (less than one year duration), without evidence of neurological involvement, requires a single dose of 2.4 million units of benzathine penicillin G. Late syphilis, including late latent and latent infections of unknown duration, requires three doses, each dose being 2.4 million units of benzathine penicillin G, spaced at one week intervals. Neurosyphilis may require inpatient treatment with aqueous crystalline penicillin G.

Stage of Syphilis	Recommended Treatment
Primary, Secondary & Early Latent	1 dose of Benzathine Penicillin G, 2.4 million units IM
Latent Syphilis	Benzathine Penicillin G, 7.2 million units total, administered as three doses of 2.4 million units IM each at one-week intervals
Tertiary Syphilis	Benzathine Penicillin G, 7.2 million units total, administered as three doses of 2.4 million units IM each at one-week intervals
Neurosyphilis	Aqueous crystalline penicillin G 18-24 million units per day, administered as 3-4 million units IV every four hours or continuous infusion for 10 to14 days

Persons infected with syphilis in whom penicillin is contradicted can be treated with alternative regimens, depending on the stage of syphilis diagnosed. Alternative regimens consist of oral doxycycline or tetracycline and require two to four weeks of treatment. Compliance with these regimens must be monitored. In pregnant women who are allergic to penicillin, desensitization and treatment with benzathine penicillin G is recommended. There is no proven alternative to penicillin in treating pregnant women with syphilis.

For the management of sex partners of infected individuals, testing and treatment depends on the stage of the index case. Presumptive treatment, along with testing, should be given to persons exposed to primary, secondary, early latent syphilis or to those exposed to individuals with latent syphilis of unknown duration with high titers (i.e. 1:32). Partners exposed to an unknown stage of syphilis should be tested and treated presumptively. Long-term sex partners of patients who have latent syphilis should be evaluated clinically and serologically for syphilis and treated on the basis of the evaluation findings.

Reporting

Syphilis is a reportable condition in North Dakota. Providers are encouraged to report all cases of infectious syphilis by phone. **Providers making a clinical diagnosis of primary or secondary syphilis should report these diagnoses to the North Dakota Department of Health immediately instead of waiting for test results and laboratory reporting to occur.** Reports can be made by calling 701.328.2378 or 800.472.2180.

Additional Information

Providers seeking more information are encouraged call the North Dakota Department of Health at 701.328.2378 or refer to the Centers for Disease Control and Prevention 2010 Sexually Transmitted Diseases Treatment Guidelines available at

www.cdc.gov/std/treatment/2010/default.htm. There is a self-study module for syphilis targeted towards providers available at: www2a.cdc.gov/stdtraining/self-study/syphilis/default.htm.

Categories of Health Alert messages:

- *Health Alert conveys the highest level of importance; warrants immediate action or attention.*
- *Health Advisory provides important information for a specific incident or situation; may not require immediate action.*
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This message is being sent to local public health units, clinics, hospitals, physicians, tribal health, North Dakota Nurses Association, North Dakota Long Term Care Association, North Dakota Healthcare Association, North Dakota Medical Association, and hospital public information officers.